

AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

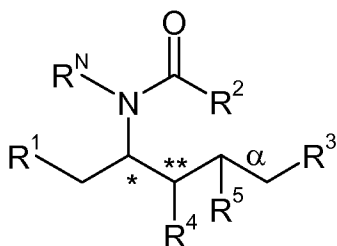
Claims 1-91. (Canceled)

92. (Currently Amended) A pharmaceutical formulation suitable for parenteral administration comprising:

(i) an amphiphilic drug; and

(ii) a short-chain sphingolipid selected from compounds of the following

formula:



wherein:

R¹ is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R¹ is independently:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted

amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-

phosphate group;

R^2 is independently C_{3-9} alkyl,

and is independently unsubstituted or substituted;

R^3 is independently C_{7-19} alkyl,

and is independently unsubstituted or substituted;

R^4 is independently -H, -OH, or -O- C_{1-4} alkyl;

R^N is independently -H or C_{1-4} alkyl;

the bond marked with an alpha (α) is independently a
single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then R^5 is -H;

if the bond marked with an alpha (α) is a single bond, then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-configuration or an
S-configuration;

the carbon atom marked (**) is independently in an R-configuration or an
S-configuration;

with the proviso that when R^1 is an O-linked saccharide group which is derived
from galactopyranose, then R^1 is D-galactopyranosyl- β 1-;

and pharmaceutically acceptable salts thereof.

Claim 93. (Canceled)

94. (Previously Presented) A pharmaceutical formulation according to claim 92,
wherein said drug is an anthracycline.

95. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is selected from: doxorubicin, idarubicin, epirubicin, aclarubicin, mitrozantrone, and daunorubicin, and salts thereof.

96. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is doxorubicin or doxorubicin hydrochloride.

97. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is an alkaloid.

98. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said drug is selected from: topotecan and camptothecin.

99. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^2 is linear.

100. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^2 is linear; and has from 0 to 3 carbon-carbon double bonds.

101. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^2 is unsubstituted or substituted with from 1 to 3 substituents selected from C_{1-4} alkyl, -OH, C_{1-4} alkoxy, -C(=O)OH, and -C(=O)O- C_{1-4} alkyl.

102. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^2 is $-(CH_2)_nCH_3$, wherein n is an integer from 4 to 8.

103. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^2 is $-(CH_2)_nCH_3$, wherein n is an integer from 6 to 8.

104. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^2 is $-(CH_2)_6CH_3$.

105. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is a double bond and R^5 is -H.

106. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is a single bond; and R^5 is -H.

107. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the bond marked alpha is a single bond; and R^5 is -OH.

108. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^3 is linear.

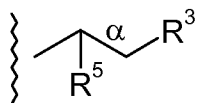
109. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^3 is linear; and has from 0 to 3 carbon-carbon double bonds.

110. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^3 is unsubstituted or substituted with from 1 to 3 substituents selected from C_{1-4} alkyl, -OH, C_{1-4} alkoxy.

111. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^3 is $-(CH_2)_nCH_3$, wherein n is an integer from 8 to 16.

112. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^3 is $-(CH_2)_{12}CH_3$.

113. (Previously Presented) A pharmaceutical formulation according to claim 92,
wherein the moiety:



is selected from the following:

- (CH₂)₈-CH₃;
- (CH₂)₁₀-CH₃;
- (CH₂)₁₂-CH₃;
- (CH₂)₁₄-CH₃;
- (CH₂)₇-CH=CH-(CH₂)₅-CH₃;
- (CH₂)₁₆-CH₃;
- (CH₂)₇-CH=CH-(CH₂)₇-CH₃;
- (CH₂)₉-CH=CH-(CH₂)₅-CH₃;
- (CH₂)₇-[CH=CH-CH₂]₂-(CH₂)₃-CH₃;
- (CH₂)₇-[CH=CH-CH₂]₃-CH₃;
- (CH₂)₄-[CH=CH-CH₂]₃-(CH₂)₃-CH₃;
- (CH₂)₇-[CH=CH]₃-(CH₂)₃-CH₃;
- (CH₂)₁₈-CH₃;
- (CH₂)₆-[CH=CH-CH₂]₂-(CH₂)₆-CH₃;
- (CH₂)₃-[CH=CH-CH₂]₃-(CH₂)₆-CH₃;
- (CH₂)₃-[CH=CH-CH₂]₄-(CH₂)₃-CH₃;

$-(\text{CH}_2)_{20}-\text{CH}_3$;

analogous of the foregoing wherein the left-most $-(\text{CH}_2)_2-$ is replaced with $-\text{CH}=\text{CH}-$; and

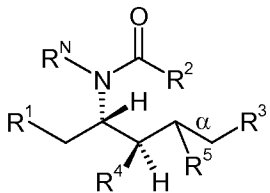
analogous of the foregoing wherein the left-most $-(\text{CH}_2)-$ is replaced with $-\text{CH}(\text{OH})-$.

114. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^4 is $-\text{H}$, $-\text{OH}$, $-\text{OMe}$, $-\text{OEt}$, $-\text{O}(\text{iPr})$, $-\text{O}(\text{nPr})$, $-\text{O}(\text{nBu})$, $-\text{O}(\text{iBu})$, $-\text{O}(\text{sBu})$, or $-\text{O}(\text{tBu})$.

115. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^4 is $-\text{OH}$.

116. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^N is $-\text{H}$, $-\text{Me}$, or $-\text{Et}$.

117. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the carbon atoms marked (*) and (**) have a configuration as shown in the following formula:



118. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^1 is an O-linked saccharide group.

119. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R¹ is an O-linked mono-, di-, or tri-saccharide group.

120. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R¹ is comprises a group or groups selected from:

arabinose, lyxose, ribose, xylose,
allose, altrose, glucose, mannose, gulose, idose, galactose, and
talose;
and derivatives thereof.

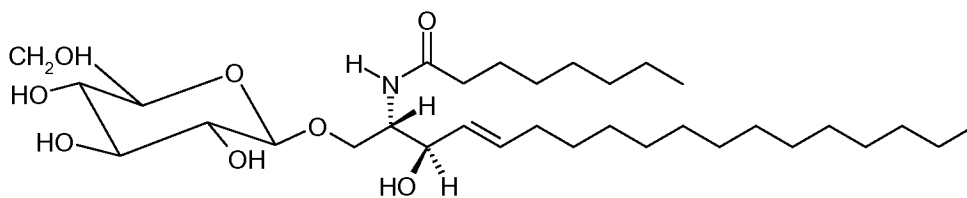
121. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R¹ is an O-linked mono-, di-, or tri-saccharide group comprising a group or groups selected from:

arabinose, lyxose, ribose, xylose,
allose, altrose, glucose, mannose, gulose, idose, galactose, talose,
sucrose, maltose, lactose, cellobiose, galabiose,
globotriaose, isoglobotriaose, mucotriaose, lactotriaose,
neolactotriaose gangliotriaose, galatritriose, mollutriaose, and antrotriaose;
and derivatives thereof.

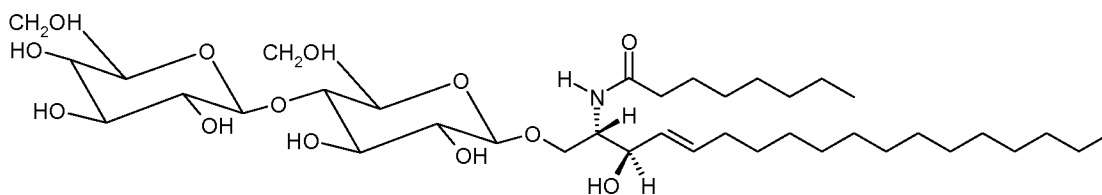
122. (Currently Amended) A pharmaceutical formulation according to claim 120, wherein said saccharide group derivatives are selected from deoxy, di-deoxy, di-deoxy-di-dehydro, methoxy [((-OMe)]], acetoxy [((-OC(=O)Me)]], carboxylic acid [((-C(=O)OH)]],

sulfuric acid $[(-OSO_3H)]$, amino-deoxy $[(-NH_2)]$, N-acetyl-amino-deoxy $[(-NHC(=O)Me)]$, or N-sulfo-amino-deoxy $(-NHS(O)_2OH)$ derivatives.

123. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula (C₈-GlcCer):



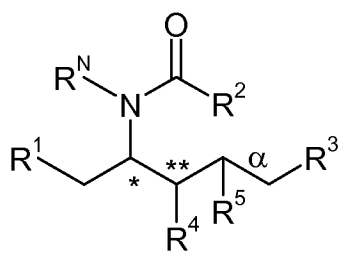
124. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula:



125. (Currently Amended) A pharmaceutical formulation comprising ~~according to claim 92,~~

(i) a drug; and

(ii) a short-chain sphingolipids selected from compounds of the following formula



wherein:

R^1 is independently an O-linked polyhydric alcohol group

R^2 is independently C_{3-9} alkyl,

and is independently unsubstituted or substituted;

R^3 is independently C_{7-19} alkyl,

and is independently unsubstituted or substituted;

R^4 is independently -H, -OH, or -O- C_{1-4} alkyl;

R^N is independently -H or C_{1-4} alkyl;

the bond marked with an alpha (α) is independently a
single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then R^5 is -H;

if the bond marked with an alpha (α) is a single bond, then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-configuration or an
S-configuration;

the carbon atom marked (**) is independently in an R-configuration or an
S-configuration;

and pharmaceutically acceptable salts thereof.

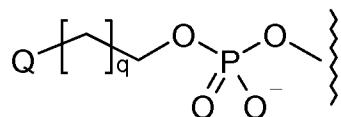
126. (Previously Presented) A pharmaceutical formulation according to claim 125, wherein R^1 comprises a group selected from: ethanediol (glycol), propanediol, butanediol, glycerol, and erythritol.

127. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R^1 is:

an O-linked (optionally N-(C₁₋₄alkyl)-substituted amino)-C₁₋₆alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)-C₁₋₆alkyl-phosphate group.

128. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R¹ is:



wherein:

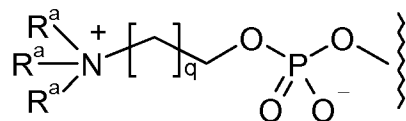
q is an integer from 0 to 5;

Q is: -NH₂, -NHR^a, -NR^a₂, or -NR^a₃⁺; or:

Q is a polyhydric alcohol group, linked via an oxygen atom;

each R^a is linear or branched saturated C₁₋₄alkyl.

129. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R¹ is:

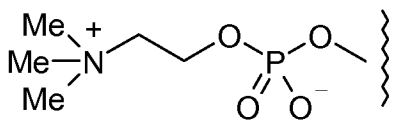


wherein:

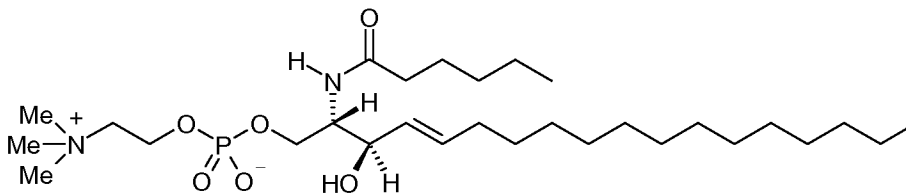
q is an integer from 0 to 5; and

each R^a is a C₁₋₄alkyl group.

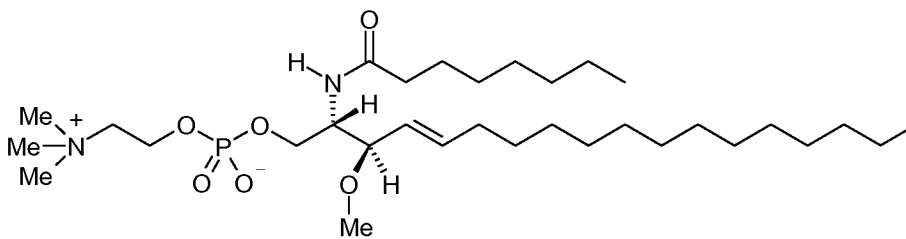
130. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein R¹ is:



131. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula ("C₆-SM"):



132. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein said short-chain sphingolipid has the following formula ("3-O-methyl-C₈-SM"):



133. (Previously Presented) A pharmaceutical formulation according to claim 128, wherein Q is a polyhydric alcohol group, linked via an oxygen atom.

134. (Previously Presented) A pharmaceutical formulation according to claim 133, wherein Q comprises a group selected from: ethanediol (glycol), propanediol, butanediol, glycerol, and erythritol.

Claim 135. (Canceled)

136. (Previously Presented) A pharmaceutical formulation according to claim 92, wherein the pharmaceutical formulation is a liposomal pharmaceutical formulation.

137. (Previously Presented) A liposomal pharmaceutical formulation according to claim 136, wherein the liposomes of the liposomal pharmaceutical formulation are prepared using a mixture of lipids comprising, at least, vesicle-forming lipids and said short-chain sphingolipid.

138. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids and said short-chain sphingolipid.

139. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phospholipids, cholesterol, and said short-chain sphingolipid.

140. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises phosphatidylcholines, cholesterol, and said short-chain sphingolipid.

141. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises fully hydrogenated soy phosphatidylcholine (HSPC), cholesterol, and said short-chain sphingolipid.

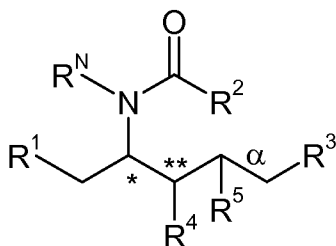
142. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids comprises dipalmitoyl-phosphatidylcholine (DPPC), cholesterol, and said short-chain sphingolipid.

143. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a vesicle-forming lipid which is derivatized with a polymer chain.

144. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises a phosphatidylethanolamine (PE) which is derivatized with polyethyleneglycol (PEG).

145. (Previously Presented) A liposomal pharmaceutical formulation according to claim 137, wherein said mixture of lipids additionally comprises N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG2000-DSPE).

146. (Currently Amended) Caelyx® or Doxil® liposomes post-inserted with a short-chain sphingolipid selected from compounds of the following formula:



wherein:

R^1 is independently:

an O-linked saccharide group; or

an O-linked polyhydric alcohol group;

or:

R^1 is independently:

an O-linked (optionally N-(C_{1-4} alkyl)-substituted amino)- C_{1-6} alkyl-phosphate group; or

an O-linked (polyhydric alcohol-substituted)- C_{1-6} alkyl-phosphate group;

R^2 is independently C_{3-9} alkyl,

and is independently unsubstituted or substituted;

R^3 is independently C_{7-19} alkyl,

and is independently unsubstituted or substituted;

R^4 is independently -H, -OH, or -O- C_{1-4} alkyl;

R^N is independently -H or C_{1-4} alkyl;

the bond marked with an alpha (α) is independently a single bond or a double bond;

if the bond marked with an alpha (α) is a double bond, then R^5 is -H;

if the bond marked with an alpha (α) is a single bond, then R^5 is -H or -OH;

the carbon atom marked (*) is independently in an R-configuration or an S-configuration;

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Atty. Ref.: 620-439
Amendment
June 1, 2010

the carbon atom marked (**) is independently in an R-configuration or an S-configuration;

with the proviso that when R¹ is an O-linked saccharide group which is derived from galactopyranose, then R¹ is D-galactopyranosyl-β1-;

and pharmaceutically acceptable salts thereof.

Claims 147-151. (Canceled)